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Lecture 12

Epidemiology of Low Birth Weight, Preterm Delivery, and Intrauterine Growth Retardation I
Low Birth Weight (LBW)

- Birth weight < 2,500 grams
- Very low birth weight < 1,500 grams

- LBW results from two processes
  - **Shortened duration of pregnancy** (preterm birth)
  - **Intrauterine growth that is less than expected** for the length of gestation: intrauterine growth retardation (IUGR) or small for gestational age (SGA)

- Multiple births have lower birth weights, so analyses must be stratified by singleton and multiple births
Birth Weight Measurement and use of Surrogate Measures

• **Birth weight on day of birth**
  – Weight drops postpartum due to neonatal diuresis, so it best measured on the day of birth

• **Delayed observation (home deliveries in LDCs)**
  – Cannot weigh infant on day of birth Use stable surrogate markers
    • Chest circumference <30 cm ~ wt <2,500 g
    • Head, calf, and mid-upper arm circumferences
Birth Weight and Intrauterine Growth Retardation

• Observed birth weight (grams)
• Birth weight for gestational age
• Percentiles of BW by GA: < 10% small for gestational age (SGA)
• Z scores
Distribution of Birth Weight in the U.S. Population

Note: 6% of births are LBW, 1% of births are VLBW
Proportional and Disproportional Intrauterine Growth Retardation

- **Proportional IUGR** - reduction in weight and length (symmetrical growth retardation, suggesting effects throughout pregnancy)

- **Disproportional IUGR** - reduction in weight more than length (growth retardation late in pregnancy)

- Measured by **Ponderal Index** (PI) = \( \frac{\text{birth weight (g)}}{\text{length (cm)}^3} \times 100 \)
Preterm Delivery

• Preterm < 37 completed weeks of gestation
• Very preterm <34 or <32 weeks (highest risk)

• Measurement
  – Fertilization (ART)
  – Last menstrual period (LMP)
  – Ultrasound
  – Maturity assessment of new born (Ballard, Dubowitz, Capurro scores). Combination of neuromuscular and developmental markers

• Subtypes
  – spontaneous preterm labor
  – preterm premature rupture of membranes (PROM)
  – induced preterm
Measurement of Gestational Age (GA)

- **Last Menstrual period (LMP)**
  - Recall Errors
    - Vary by education, literacy, numeracy
  - Women not menstruating
    - overestimate GA, underestimate PTD
      - lactating
      - recent spontaneous abortion
      - recent delivery
  - Individual variability in length of menstrual cycle
    - Long cycles: underestimate GA, overestimate PTD?
    - Short cycles: overestimate GA, underestimate PTD?
  - Bleeding during pregnancy
    - Underestimate GA (mistaken for LMP)
Classification of LBW/PTD

<table>
<thead>
<tr>
<th>GA</th>
<th>LBW</th>
<th>NORMAL BW</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 37 weeks</td>
<td>IUGR</td>
<td>Normal</td>
</tr>
<tr>
<td>&lt; 37 weeks</td>
<td>Preterm and/or IUGR</td>
<td>Preterm</td>
</tr>
</tbody>
</table>
PTD and IUGR as Determinants of LBW

- LBW infant born at 40 weeks results from IUGR
- Preterm infant may be LBW, but have an appropriate weight for its gestational age
  - LBW only because it was born early
- Preterm infant may also be growth retarded
  - LBW because of both its shortened gestation and its growth retardation
Live Births by Birth Weight, U.S., 2002

- Not LBW: 92.2%
- LBW: 7.8%

Source: NCHS (2002), Final natality data
Live Births by Gestational Age, U.S., 2002

Total Births: 4,021,726

Not Preterm: 87.9%

Preterm: 12.1%

Source: NCHS (2002), Final natality data
Low Birth Weight Worldwide

- LBW = 16.4% in developing countries (20.5 million infants/year)
- Term LBW = 11% (13.7 million infants)
- IUGR = 23.8% (30 million infants)
- Distribution of burden:
  - 75% in Asia (mostly south-central Asia)
  - 20% in Africa
  - 5% in Latin America

Onis, M. et al., EJCN, 1998
### Prevalence of LBW, IUGR and PTD in Developing Countries

<table>
<thead>
<tr>
<th></th>
<th>Argentina</th>
<th>Malawi</th>
<th>Nepal</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW %</td>
<td>6.3</td>
<td>11.6</td>
<td>22.3</td>
</tr>
<tr>
<td>IUGR %</td>
<td>9.7</td>
<td>26.1</td>
<td>42.7</td>
</tr>
<tr>
<td>PTD %</td>
<td>7.2</td>
<td>8.2</td>
<td>21.8</td>
</tr>
</tbody>
</table>

WHO collaborative study of pregnancy outcomes, A. Kelly et al., 1996
Proportion of LBW due to PTD & IUGR: International Comparisons

- **Developed countries**: preterm 75%, IUGR 25%
- **Developing countries**: preterm 25%, IUGR 75%
- Based on meta-analysis of studies, mainly from Latin America, problematic measurement of gestational age

- **Africa (Rakai)**
  - All LBW 11.0%
  - LBW/IUGR 7.4%
  - LBW/PTD 3.6%
  - 67% IUGR, 33% PTD
Fetal growth in early pregnancy and LBW

- Hypothesis that poor placental function in 1st trimester can cause LBW.

- Use crown-rump length based on ultrasound to estimate growth in the first trimester, in women with known dates of conception based on LMP or assisted reproduction (IVF, intrauterine insemination) expressed observed to expected days of gestation.
Fetal growth in 1\textsuperscript{st} trimester assessed by LMP and crown-rump length and outcomes at birth \cite{SmithNEJM1998}

4229 singleton pregnancies with LMP and 1\textsuperscript{st} trimester ultrasound

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Adjusted OR (CI) associated with smaller than expected crown-rump length</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW</td>
<td>1.7 (1.2-2.3)</td>
</tr>
<tr>
<td>SGA &lt;5%</td>
<td>2.8 (1.9-4.3)</td>
</tr>
<tr>
<td>PTD 24-32 wk</td>
<td>2.0 (1.1-4.0)</td>
</tr>
</tbody>
</table>
1st trimester growth based on LMP and LBW


Figure 1. Proportion of Infants with Birth Weights of Less Than 2500 g According to the Difference between Observed and Expected First-Trimester Crown–Rump Lengths. P values are for the comparison with the group with normal crown–rump length (−1 to +1 day) by Fisher’s exact test (two-tailed). The proportion of infants with low birth weight in the pooled group for whom the difference was −9 to +6 days was not significantly different from the proportion of infants for whom the difference was less than −9 days (32 of 492; P = 0.12) or greater than +6 days (12 of 63; P = 0.77). The crown–rump length was expressed as equivalent days of growth.
SGA associated with lower 1\textsuperscript{st} trimester growth in women with ART (Bukowski BMJ 2007)

Based on precise dates of Conception, poor fetal Growth in the 1\textsuperscript{st} trimester Increased the risk of SGA

Fig 2 | Proportion of small for gestational age (SGA) neonates by size of $\Delta$GA discrepancy (difference between observed and expected size of fetus in first trimester of pregnancy). Proportion (±SE) of SGA neonates and proportion of SGA neonates predicted by multivariable logistic regression are plotted by size of $\Delta$GA discrepancy

Birth Weight and Gestational Age Effects on Mortality and Morbidity

• Birth weight and gestational age are predictors of infant mortality

• **Low Birth Weight**
  – Moderate LBW infant mortality RR ~ 5 vs. normal birth weight
  – VLBW infant mortality RR ~ 100 vs. normal-weight infants

• **Preterm Delivery**
  – 70% of perinatal deaths are PTD
  – 50% of long-term neurologic morbidity is PTD
  – Most serious morbidity/mortality in PTD < 32 weeks and very low birth weight (VLBW < 1500 g)
Birth Weight and Gestational Age Effects on Infant Mortality

- Are infants at high risk of dying because they are small or because they are preterm?

- Gestational age is in the causal pathway leading to birth weight
Birth Weight and Perinatal Mortality

Mortality Rate per 1,000 births

Birth Weight
Early Neonatal Deaths/100 Livebirths by PTD, LBW and SGA

Mortality per 1,000 Live Births

Birth Weight in Relation to Morbidity and Mortality Among Newborn Infants

**Figure 1.** Incidence of Respiratory Distress and Neonatal Death among 12,317 Preterm Infants (Born at 24 to 36 Weeks of Gestation), According to Birth-Weight Percentile.

**Figure 2.** Incidence of Respiratory Distress among 12,317 Preterm Infants, According to Birth-Weight Percentile after Stratification According to Gestational Age (28 through 30 Weeks, 31 or 32 Weeks, 33 or 34 Weeks, and 35 or 36 Weeks).

Does LBW affect long-term health in adulthood? (Life-course effects)

• **Barker hypothesis** *(Am J Clin Nutr 2000;71:1344S)*
  - Fetal nutrition determines fetal growth and birth weight
  - Impaired fetal nutrition reflected by LBW can increase the risks of adult morbidity due to cardiovascular disease, toxemia, chronic obstructive pulmonary disease.
  - Is this impaired intrauterine growth or some common genetic mechanism (e.g. fetal insulin hypothesis)?
  - Need birth weight or SGA from early records
**Mortality from Ischemic Heart Disease, by quartiles of Birth Weight for Gestational Age. Singleton Live Male Births 1915-29 Uppsala Academic Hospital**

<table>
<thead>
<tr>
<th>Birth Weight for Gestational Age</th>
<th>Fourth (No of Deaths)</th>
<th>Adjusted Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{st} (n=203)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2\textsuperscript{nd} (n=173)</td>
<td>0.80 (0.62-1.04)</td>
<td></td>
</tr>
<tr>
<td>3\textsuperscript{rd} (n=127)</td>
<td>0.61 (*0.43-0.86)</td>
<td></td>
</tr>
<tr>
<td>4\textsuperscript{th} (n=144)</td>
<td>0.67 (0.43-1.02)</td>
<td></td>
</tr>
</tbody>
</table>

p-value for trend 0.003

## Hypertension During Pregnancy by Maternal Birth Status

<table>
<thead>
<tr>
<th>Maternal Birth Status</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA</td>
<td>1.7 (1.1-2.6)</td>
<td>1.8 (1.1-2.8)</td>
</tr>
<tr>
<td>Not SGA</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Preterm</td>
<td>1.3 (0.8-2.0)</td>
<td>1.5 (0.96-2.5)</td>
</tr>
<tr>
<td>Not preterm</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Genetic and familial factors affecting birth weight and gestational age

- Possible genetic characteristics of fetus or maternal genetic factors may affect fetal growth
  - Studies in twins and offspring of twins suggest ~ 40-50% of birth weight variability due to fetal genes (Magnus Clin Genet 1984;25:15)
  - Studies of familial correlations estimate genetic factors account for 31% of birth weight and 11% of gestational age variation (Lunde Am J Epidemiol 2007;165:734)
  - Genetic studies have linked genes on chromosome 6q to fetal growth (Arya Hum Mol Genet 2006;15:1569) and polymorphisms to SGA and pre-eclampsia in black women (Wang Am J Hum Genet 2006;78:770)
## Infant Birth Weight and Gestational Age by Maternal Birth Weight

<table>
<thead>
<tr>
<th>Mother’s birth weight (lb)</th>
<th>Infant</th>
<th>2-3.9 (n=24)</th>
<th>4-5.9 (n=173)</th>
<th>6-7.9 (n=751)</th>
<th>≥8 (n=400)</th>
<th>p(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Birth Weight, g</strong></td>
<td></td>
<td>3,204 0 (0)</td>
<td>3,091 18 (10)</td>
<td>3,267 39 (5)</td>
<td>3,415 11 (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>No (%) LBW</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Mean length of gestation</strong></td>
<td></td>
<td>39.7 2 (8)</td>
<td>39.8 8 (5)</td>
<td>39.9 44 (6)</td>
<td>40.0 14 (4)</td>
<td>0.77</td>
</tr>
<tr>
<td><strong>No (%) PTD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.30</td>
</tr>
</tbody>
</table>

\(a\) – F test for comparison of means, \(\chi^2\) test for comparison of percentages

Maternal Birth Weight Effects on Infant birth weight (Intergenerational)

- A mother’s own birth weight predicts her infant’s birth weight
- For every 100 g increase in maternal BW, infant BW increases 10-20 g
- Equivocal evidence of intergenerational effect on preterm delivery
## Risk of Poor Pregnancy Outcomes by Maternal Pregnancy Outcome

<table>
<thead>
<tr>
<th>Maternal status</th>
<th>Odds Ratio (OR) of poor pregnancy outcome among infants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SGA</td>
</tr>
<tr>
<td>SGA</td>
<td>2.21 (1.41, 3.48)</td>
</tr>
<tr>
<td>PTD</td>
<td>2.96 (1.47, 5.94)</td>
</tr>
</tbody>
</table>

Race/Ethnicity as Determinants of Poor Pregnancy Outcomes

- In the U.S., black infant mortality is twice that of white infants
- Higher LBW rates among blacks are primarily the result of higher preterm delivery rates
  - Black women experience twice the rate of preterm delivery of white women and these differences are greatest for the most vulnerable newborns (< 1500 gms or < 32 weeks)
- Higher rates of IUGR among black infants also contribute to the higher rates of LBW
Race/Ethnicity and Poor Pregnancy Outcomes

• Genetic selection? (teleologic argument that smaller babies confer protection from obstructed labor, “small is beautiful”)

• Poorer pre-pregnancy health of minority populations
  – Higher rates of infection? (Higher prevalence of GTIs, especially BV in African American women)
  – Higher rates of obesity and chronic disease
Racial Differences in LBW: African-American vs. African-born Blacks

• U.S.-born black women
  – LBW = 13.2%
• African-born black women (resident in US)
  – LBW = 7.2%
• White women
  – LBW = 4.3%
  – Cannot be due to “race” alone

  – David and Collins NEJM 1997;337:1209
Race/Ethnicity and Poor Pregnancy Outcomes

• Adjustment for traditional risk factors has failed to account for observed racial/ethnic differences

• Why?
  – Education level may not represent the same quality of life and opportunities for success for blacks and whites
  – Blacks and whites with college educations do not achieve similar levels of wealth

Neonatal mortality, by gestational age, for Black (•) and for White (o) infants in the United States. Solid lines denote data for 1989; dashed lines are for 1997. Data shown are for <37 weeks of gestation only.

Parental Race and LBW

- Black mother/black father  LBW = 11.7
- Black mother/white father  LBW = 8.3
  - Adj RR = 0.78 (0.68-0.73)

- White mother/white father  LBW = 4.9
- White mother/black father  LBW = 6.4
  - Adj RR = 1.05 (1.03-1.08)

- Cannot differentiate race from SES
  - Parker *Epidemiol* 2000;11:242
Race and recurrence of PTD
(Kitska Am J Ob Gynecol 2007;196:131)

• Cohort of 2 or more singleton births between 1989-97

• 368,633 singleton deliveries, 63223 black

• Looked at risk of recurrence and timing of recurrent PTDs, adjusting for sociodemographic and health
### Risks of Black/white PTD

<table>
<thead>
<tr>
<th>PTD 20-34 weeks</th>
<th>OR black/white</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated PTD</td>
<td>2.41 (2.31-2.51)</td>
</tr>
<tr>
<td>Recurrent PTD crude</td>
<td>6.53 (6.14-6.94)</td>
</tr>
<tr>
<td>Recurrent PTD adjusted</td>
<td>4.11 (3.78-4.47)</td>
</tr>
</tbody>
</table>
Rates and risks of PTD 20-34 weeks by outcome of prior pregnancy and race

Risk of subsequent preterm birth in Missouri to a mother with either an initial preterm or full-term birth, according to race, 1989-1997.

<table>
<thead>
<tr>
<th></th>
<th>Initial preterm</th>
<th>Initial full-term</th>
<th>OR</th>
<th>CI (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All births</td>
<td>12.34</td>
<td>3.59</td>
<td>3.78</td>
<td>3.66-3.91</td>
</tr>
<tr>
<td>Black</td>
<td>21.50</td>
<td>8.51</td>
<td>3.68</td>
<td>3.53-3.85</td>
</tr>
<tr>
<td>White</td>
<td>9.18</td>
<td>2.49</td>
<td>2.53</td>
<td>2.40-2.66</td>
</tr>
</tbody>
</table>

Race/Ethnicity and Poor Pregnancy Outcomes

- Some traditional risk factors have been operationalized in a simplistic fashion
- Look beyond traditional factors
  - Psychosocial factors and physical activity
  - Home/neighborhood or work environment may help explain the race “gap” in pregnancy outcomes
Race/Ethnicity

Measurement of race and ethnicity is fraught with problems

- Frequently interpreted as a biological characteristic when it is a socially determined characteristic
- Definition of “race” problematic (self-reported on birth certificates, misclassification, mixed race)
- However, self-reported ethnicity reflects geographic ancestry when evaluated by genetic markers, and gene frequencies vary between geographic isolates
Maternal Age and LBW by Race

Proportion of low birthweight (<2500 g) and very low birthweight (<1500 g) births by maternal age and ethnicity

Figure 2 Odds ratios of delivering low birthweight for black mothers compared with white mothers by maternal age, derived from three models. Chicago, 1994–1996

Black mothers Have higher LBW At all ages and level Of poverty

Maternal Age and Preterm Delivery

- Younger age at first birth associated with increased PTD. Is it immaturity or social effect?
- Older age also associated with PTD

<table>
<thead>
<tr>
<th>Age</th>
<th>PTD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>11.5</td>
</tr>
<tr>
<td>20-24</td>
<td>6.3</td>
</tr>
<tr>
<td>25-34</td>
<td>5.2</td>
</tr>
<tr>
<td>35+</td>
<td>9.0</td>
</tr>
</tbody>
</table>
Adolescent Pregnancy and PTD

- Younger adolescents have increased risk of PTD and Very Preterm Delivery (VPTD)

<table>
<thead>
<tr>
<th>Age</th>
<th>33-36 wks (%)</th>
<th>≤32 wks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-15</td>
<td>9.0</td>
<td>5.9</td>
</tr>
<tr>
<td>16-17</td>
<td>7.3</td>
<td>2.5</td>
</tr>
<tr>
<td>18-19</td>
<td>5.9</td>
<td>1.7</td>
</tr>
<tr>
<td>20-24</td>
<td>4.5</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Olausson *Br J Ob Gynecol* 1999;106:116
Parity and Pregnancy Outcomes

- Low and high parity associated with both LBW and PTD

<table>
<thead>
<tr>
<th>Parity</th>
<th>LBW (%)</th>
<th>PTD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7.6</td>
<td>4.7</td>
</tr>
<tr>
<td>1</td>
<td>5.4</td>
<td>3.9</td>
</tr>
<tr>
<td>2-3</td>
<td>6.8</td>
<td>5.2</td>
</tr>
<tr>
<td>4+</td>
<td>7.4</td>
<td>5.5</td>
</tr>
</tbody>
</table>
Age, Parity and Pregnancy Outcomes

• Maternal age may be associated with other factors independently associated with increased risk of poor pregnancy outcomes
  – First pregnancy in older mothers may explain increased risk rather than age *per se*
  – Older mothers may have more chronic medical problems
  – Young motherhood also associated with lower SES, nutritional inadequacy, lower prepregnancy weight and pregnancy weight gain, and higher stress
Birth Spacing and Poor Pregnancy Outcomes

• Do short intervals between subsequent pregnancies lead to impaired fetal nutrition and higher risk of LBW, PTD, SGA?
• Is there an optimal interval between births?
Prevalence of Adverse Perinatal Outcomes According to Interpregnancy Interval. 173,205 Singleton Infants

### Short (<12 months) Interpregnancy Intervals and Low Birth Weight by ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Low Birth Weight (&lt;2.5 kg)</th>
<th>Interval:</th>
<th>OR</th>
<th>95% CI</th>
<th>Interval:</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt; 6 months</td>
<td></td>
<td></td>
<td>6-12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African Americans</td>
<td></td>
<td>1.34</td>
<td>95% CI</td>
<td>1.30-1.37</td>
<td>0.98</td>
<td>95% CI</td>
<td>0.96-1.00</td>
</tr>
<tr>
<td>Mexicans</td>
<td></td>
<td>1.38</td>
<td>95% CI</td>
<td>1.32-1.44</td>
<td>0.98</td>
<td>95% CI</td>
<td>0.94-1.02</td>
</tr>
<tr>
<td>Native Americans</td>
<td></td>
<td>1.07</td>
<td>95% CI</td>
<td>0.91-1.26</td>
<td>0.92</td>
<td>95% CI</td>
<td>0.79-1.07</td>
</tr>
<tr>
<td>Non-Hispanic Whites</td>
<td></td>
<td>1.28</td>
<td>95% CI</td>
<td>1.26-1.31</td>
<td>0.98</td>
<td>95% CI</td>
<td>0.96-1.00</td>
</tr>
<tr>
<td>Puerto Ricans</td>
<td></td>
<td>1.28</td>
<td>95% CI</td>
<td>1.13-1.44</td>
<td>1.02</td>
<td>95% CI</td>
<td>0.90-1.15</td>
</tr>
</tbody>
</table>

Stress and Pregnancy

- Physiology
- Physical stressors
- Psychogenic stress
- Evidence of associations with PTD, PROM
- Some evidence of association with LBW, IUGR
Pathway for Action of Placental Corticotropin Releasing Hormone on Parturition

Maternal Stress

<table>
<thead>
<tr>
<th>Cortisol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin II</td>
</tr>
<tr>
<td>Norepinephrine</td>
</tr>
<tr>
<td>ADH</td>
</tr>
<tr>
<td>acetylcholine</td>
</tr>
</tbody>
</table>

Fetal Stress

<table>
<thead>
<tr>
<th>CRH</th>
</tr>
</thead>
<tbody>
<tr>
<td>enhanced fetal lung maturity</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pg</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Membranes</td>
</tr>
<tr>
<td>Placenta</td>
</tr>
<tr>
<td>decidua</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Contractns</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROM</td>
</tr>
<tr>
<td>Cx Change</td>
</tr>
</tbody>
</table>

ADH – Antidiuretic hormone
CRH – corticotropin releasing hormone
Pg – prostaglandin
Ctx – contractions
ROM – rupture of membranes
Cx – cervix

Maternal CRH by Week of Gestation

Women who delivered prematurely
Women who delivered at term
Women who delivered late

Smith R. Scientific American 1999; March:68.
Physical Stressors

• Infection
• Physical
  – Heat, noise exposures at work
  – Standing on the job
  – Heavy lifting
  – violence
• Nutritional
Physical Stress

- **Physical stress in the workplace**
  PTD risk among prospective cohort of working Danish women (Henriksen, Br J Obstet Gynaecol, 1995):
  - >5 hours standing and walking OR for PTD = 3.3 (1.4, 8.0)

- **Physical activity**
  - Increased risk for physical activities of daily living
    - Climbed stairs ≥10x/day, PTD OR = 1.60 (1.05, 2.46)
  - Decreased risk for leisure-time exercise,
    - Exercise ≥60x in 1st-2nd trimester, PTD OR = 0.51 (0.27, 0.95)
Psychosocial Stress

- Psychosocial measures
  - Life events
  - Job demands vs. control
  - Time pressures
  - Interpersonal relationships/social support

- Chronic vs. Acute
- Timing in pregnancy
Measurement of Acute Antenatal Stress

• Life events scales
  • Nature of event (e.g. job loss, marital disruption)
  • Timing, # events
  • Objective assessment of events

• Perceptions, subjectivity of response to life events (Lazarus)
  • **Stressors** are the sources of stress (can be quantified)
  • **Stress** is the perceived experience and may vary with personality type, social setting etc. (Hard to quantify)
• Social support
Stress measurement

• Likert scales for psychosocial domains (Assessment of Psychosocial Status in Pregnancy, NICHD)
  – Anxiety
  – Self-esteem
  – Mastery
  – Depression
  – Stress
Measurement of Antenatal Stress: Recall Bias

- Subjective nature of information
- Information obtained after completed pregnancy biased by anxiety (e.g., having a PTD)
- Need measurements during pregnancy prior to outcome
Prospective study of stress and PTD

• 1962 women assessed during pregnancy
• Risks of PTD
  – High pregnancy related anxiety RR = 1.4 (1.0-2.0)
  – Negative life events RR = 1.8 (1.2-2.7)
  – Perceived racial discrimination RR = 1.4 (1.0-2.0)

(Dole Amer J Epidemiol 2003; 157:14)
Stress and LBW/IUGR

- **Exposure to stressors and race**
  - African-American women, OR=1.52 (1.33, 1.91)
  - Caucasian women, OR=0.48 (0.01, 1.37)

- **Psychosocial resources**
  Prospective cohort in Sweden – SGA risk (Dejin-Karlsson, BJOG, 2000)
  - Poor social network index, OR = 3.3 (1.6, 6.7)
  - Poor social support index, OR = 2.7 (1.3, 5.6)
Acute Stress and Modifiers of Response I

• **Personality and cognitive response**
  – Sweden at time of Chernobyl: Women with high psychic and somatic anxiety scores had shorter gestation, but women with low scores had no effect (Levi *J Psychosom Obstet Gynecol* 1989;10:221)

  – Positive correlation between PTD and “psychopathologic score” (negative attitudes towards pregnancy) (Mamelle *AJE* 1989;130:989)
Acute Stress and Modifiers of Response

• **Social Support**
  – Some observational studies suggest social support can mitigate effects of life events
  – Randomized trial of improved social support showed no benefit (Spencer *Br J Obstet Gynaecol* 1989;96:281)

• **Nutritional status**
  – Poor psychosocial profile increased risk of IUGR among low-income, minority U.S. women who were thin
  – Poor psychosocial profile:
    • Women with BMI<median, RR=2.11 (1.47, 3.04)
    • Women with BMI≥median, RR=1.20 (0.73, 1.98)
      (Cliver, *Obstet Gynecol* 1992;80:262)
Measurement of Chronic Antenatal Stress

- Chronic Stressors/Stress
  - Poverty
  - Racism
  - Family (spouse, children)
Biomarkers

• Measure hormonal response to stress to avoid subjectivity and to capture cognitive response
  – Noradrenaline
  – Salivary alpha amylase
  – CrH
  – Associations between biochemical markers and increased risk of PTD and LBW
  – Problem elevation of biomarkers occurs late in pregnancy and cannot be used for prevention
Corticotropin-Releasing Hormone and Parturition

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study population</th>
<th>Key CRH findings Study pop’n</th>
<th>Normal</th>
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</thead>
<tbody>
<tr>
<td>Warren et al. 1992</td>
<td>Preterm labor (PTL)</td>
<td>1240 ± 320</td>
<td>600 ± 67</td>
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<tr>
<td>Ruth et al. 1993</td>
<td>Preeclampsia, PROM</td>
<td>24.1 (14.2-67)</td>
<td>6.35 (1.0-27.5)</td>
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<tr>
<td>Tropper et al. 1992</td>
<td>Preeclampsia, PROM, PTL</td>
<td>1058 ± 184</td>
<td>456 ± 71</td>
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